Clarithromycin and azithromycin, newer macrolide antibiotics with minimal effects on hepatic cytochrome P-450, have not been evaluated for their interactions with terfenadine. The possible drug interactions between fluconazole and terfenadine have not yet been characterized. The concomitant administration of these agents with terfenadine is not recommended until more data are available. Other clinical conditions that alone may prolong the QT interval and possibly increase the likelihood of terfenadine cardiotoxicity include hypokalemia, hypomagnesemia, hypocalcemia, and the congenital QT syndrome.

Astemizole, a longer-acting nonsedating antihistamine, has been reported to cause a wide spectrum of cardiac dysrhythmias in patients with acute overdose but rarely at recommended dosages. In addition to torsades de pointes and other ventricular tachyarrhythmias with prolonged QTc interval, first- and second-degree atrioventricular blocks and bundle branch blocks have been described, the last particularly in children. Because of the long half-life of astemizole metabolites, several days of cardiac monitoring and supportive therapy are recommended in patients with overdose with this agent.

Because of more limited experience with two other second-generation antihistamines soon to be available in the United States, cetirizine and loratidine, the spectrum of cardiac toxicity with these agents is less clear. Cetirizine is excreted largely unchanged in the urine, and patients with impaired renal function could have prolonged half-lifes for this drug. Loratidine, like astemizole and terfenadine, is metabolized by the liver. In any case, careful consideration to possible drug interactions and long-term clinical conditions should be given before prescribing second-generation antihistamines.

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REFERENCES

Honig PK, Woosley RL, Zamani K, Conner DP, Catilena LR Jr: Changes in the pharmacokinetics and electrocardiographic pharmacodynamics of terfenadine with concomitant administration of erythromycin. Clin Pharmacol Ther 1992; 52:231-238

Simons FE, Simons KJ: Second-generation H_1-receptor antagonists. Ann Allergy 1991; 66:5-21

Tobin JR, Doyle TP, Ackerman AD, Brenner JI: Astemizole-induced cardiac conduction disturbances in a child. JAMA 1991; 266:2737-2740

Vocal Cord Dysfunction Presenting as Asthma

WHEEZING OCCURS IN various organic lung diseases as a result of reversible or irreversible airway narrowing, localized endobronchial disease (such as tumor or sarcoidosis), and diffuse or localized lung disease (such as pulmonary edema, lymphangitic disease, or pulmonary embolism). Vocal cord dysfunction, a recently described syndrome that presents as asthma, is an uncommon but important asthma impersonator that should be included in every physician's differential diagnosis of asthma.

The pathophysiologic mechanism involved in vocal cord dysfunction is a dysfunction of the larynx in which the vocal cords are inappropriately adducted during inspiration, expiration, or both. The sound produced can be similar to asthmatic wheezing, and patients may be mistakenly diagnosed and treated for asthma. Missing this diagnosis has serious consequences, for many patients have received tracheotomies or been aggressively treated for asthma with systemic corticosteroids, producing iatrogenic Cushing's syndrome.

The clinical presentation is often dramatic, with a frightened patient reporting to an emergency department or physician's office with one of many attacks of profound wheezing and dyspnea. Patients are typically young women between the ages of 20 and 40. The syndrome has recently been reported in children as well. On examination, there are inspiratory and expiratory wheezes loudest over the larynx and less well transmitted to the chest wall. Arterial blood gas values are usually normal, as opposed to the hypoxemia seen in acute asthma, and pulmonary function studies show pronounced variability in spirometric test results. Laryngoscopy during wheezing shows almost complete adduction of the vocal cords, with the glottis reduced to a small posterior diamond-shaped opening. This finding and the wheezing it produces can be reversed by asking the patient to cough or breathe in a panting manner. If seen when an attack is not occurring, the patient will often report that the wheezing comes from the throat and not the chest.

Because true asthma and vocal cord dysfunction can coexist, the use of a methacholine challenge test to evaluate a patient's bronchial hyperresponsiveness should be done in most patients. A flow-volume loop characteristic of extrathoracic airways obstruction can be helpful.

The cause of the condition is not clear, but a hypothesis is that "suggestion" mediated by the vagus nerve may alter the laryngeal tone and lower the threshold for stimuli to produce vocal cord spasm. Recently there have been several reports of cases of vocal cord dysfunction associated with gastroesophageal reflux, which reversed with treatment of the reflux.

Vocal cord dysfunction presenting as asthma can have a psychological basis. The operative mechanisms that come into play include conversion reactions associated with a variety of conditions, such as depression, a passive-dependent personality, and somatization disorder. These patients do not knowingly control their illness for secondary gain, and therefore it is not considered malingering. Therapy consists of a multidisciplinary approach including the physician, psychiatrist, and speech therapist. The physician's role is to inform the patient of the findings, especially the absence of diseases such as asthma, and to explain the nature of the condition. Patients often express a positive reaction to the initial explanation, and such a reaction often implies a good prognosis.

It must be recalled that vocal cord dysfunction and true asthma may coexist; therefore, in an acute attack, the patient should be treated for asthma unless there is absolute proof that asthma is not the cause of the symptoms.

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REFERENCES

Goldman J, Muers M: Vocal cord dysfunction and wheezing. Thorax 1991; 46:401-404

Meltzer EO, Orgel HA, Kemp JP, et al: Vocal cord dysfunction in a child with asthma. J Asthma 1991; 28:141-145

Sharon GE: Vocal Cord Dysfunction Increased From Esophageal Reflux, Abstract #42. Presented at the American College of Allergy and Immunology meeting, November 1992, Chicago, Illinois

Sinusitis

SINUSITIS OFTEN EVADES RECOGNITION because of its protean and sometimes elusive clinical manifestations and because of the relative inaccessibility of the paranasal sinuses to direct visualization. Interest in sinus disease has been renewed by an increased awareness of its prevalence, possible ramifications (such as refractory asthma), and possible complications (such as intraorbital or intracranial extension). Recent progress toward understanding the cause and pathophysiology of sinusitis has been accompanied by important advances in diagnostic imaging and in medical and surgical therapy.

Recently it has been established that most sinus disease in adults and children involves the maxillary and anterior ethmoidal sinuses, both sets of which are present at birth and, along with the frontal sinuses, drain into the middle meatus. Disease of the sphenoidal and posterior ethmoidal sinuses, which drain through the superior meatus, and of the frontal sinuses is less common, but diagnostic sinus imaging always should include the frontal sinuses in patients older than 3 years and frontal plus sphenoidal sinuses in those older than 8 years.

New evidence from computed tomographic (CT) studies underscores the importance of ostial occlusion in the cause of sinusitis. This is especially apparent in the predisposition to ethmoid sinusitis, where even minimal mucosal edema, mucociliary stasis, or anatomic obstruction threatens the patency of the 1 to 2 mm in diameter ethmoidal air-cell ostia. Moreover, disease involving the anterior ethmoidal bullae and maxillary outflow tract (collectively called the ostiomeatal complex) predisposes to disease of the ipsilateral frontal, ethmoidal, and maxillary sinuses by obstructing their common drainage pathway through the middle meatus.

Acute sinusitis is most frequently a complication of upper respiratory tract infection. Allergy and, less so, irritant exposure (cigarette smoke), immunodeficiency, and mechanical obstruction (polyp, tumor, granuloma, adenoidal hypertrophy, foreign body, and septal deviation) underlie most instances of recurrent acute and chronic sinusitis. An important but less common occurrence is that sinusitis may be the first sign of systemic diseases such as Wegener's granulomatosis or diseases associated with mucus stasis, such as cystic fibrosis and mucociliary dyskinesia syndromes. Sinusitis should be suspected when signs and symptoms of upper respiratory tract infection persist longer than seven to ten days. The most common signs are cough, nasal discharge, fetor oris, periorbital swelling, and fever, with symptoms of headache, facial pain, odontalgia, and hyposmia reported by verbal children and adults. A sizable proportion of adults and children (40% to 75%) with asthma present with an often recalcitrant asthmatic exacerbation in association with sinusitis. In most patients, the resolution of sinusitis is accompanied by substantial lessening of asthma and a consequent reduction in the need for bronchodilator and corticosteroid use.

Flexible fiberoptic rhinoscopy, done in cooperative older children and in adults after the topical application of a vasoconstrictor and anesthetic, has permitted direct visualization of intranasal anatomy inaccessible to anterior rhinoscopy. The efflux of mucopurulent secretions from the middle meatus is a reliable indicator of acute sinusitis. Transillumination is less helpful because near-complete unilateral opacification is required to confirm the diagnosis. Similarly, nasal cytologic examination is relatively nonspecific. Coronal CT scanning is superseding radiography as the diagnostic imaging modality of choice and provides an excellent demonstration of bony landmarks and obstructing lesions of the ostiomeatal complex. Magnetic resonance imaging, while not producing satisfactory resolution of bony detail, is superior to CT in distinguishing soft-tissue characteristics. Ultrasonography has fallen into general disfavor because of its low sensitivity and specificity. Recent studies record as much as a 75% discordance rate between plain films and coronal CT, with conventional radiography substantially underestimating both the presence and extent of sinus disease. In many institutions, the cost of a limited coronal sinus CT study approximates that of a plain film sinus series. Because many cases of sinusitis can be diagnosed and treated on the basis of clinical suspicion alone, it is increasingly recommended that CT scanning as the sole imaging study be reserved for clinically suspected sinusitis that is refractory to medical management.

Culture of sinus aspirates obtained by transnasal maxillary antral puncture is far more predictive of actual intrasinus infection than nasal or nasopharyngeal cultures, but is impractical in routine clinical settings. A rational selection of empiric antimicrobial therapy may be guided by recent studies. *Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis* account for most cases of acute and chronic uncomplicated sinusitis in children and adults. α-Hemolytic streptococci and *Staphylococcus aureus* are identified occasionally in cases of long-standing or severe disease. Whereas anaerobes are rarer causes of sinusitis in children, *Bacteroides* species, almost half of which are β-lactamase–producing, and anaerobic cocci may cause most cases of chronic sinusitis in adults. In areas where the prevalence of β-lactamase–producing pathogens is low, acute sinusitis is appropriately treated with amoxicillin for three to four weeks.

Should clinical improvement not occur within 48 hours of starting first-line antibiotic therapy, a β-lactamase–resistant agent should be substituted. These include the combinations of amoxicillin and clavulanate potassium, erythromycin ethylsuccinate and sulfisoxazole, cefaclor (which is inactivated by β-lactamases of most *M catarrhalis* and *H influenzae*), trimethoprim and sul-